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REMARKS

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page(s) is captioned "Version With Markings To Show Changes Made."

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADEIN THE SPECIFICATION

Page 1, before the first line, please insert as a separate paragraph:

This application is the US national phase of international application

PCT/GB00/03575 filed 18 September 2000, which designated the US.

IN THE CLAIMS

3. A vaccine according to claim 1 or 2 wherein the heterologous antigen can induce immunogenicity against a pathogenic microorganism, optionally a heterologous antigen specific for a mucosa colonising pathogen or pathogen entering the body via the mucosa, such as via the oral route.

4. A vaccine according to ~~any of the preceding claims~~ 1 wherein the heterologous antigen induces immunogenicity against a pathogenic microorganism colonising the gastrointestinal tract.

5. A vaccine according to ~~any of the preceding claims~~ 1 wherein the pathogenic microorganism is herpes virus, rubella virus, influenza virus, mumps virus, measles virus, poliomyelitis Virus, rotavirus, respiratory syncytial virus, *Campylobacter* species, *Chiamydial* organisms, species of the genus *Cryptosporidium*, cytomegalovirus, human immounodeficiency virus, *Actinomyces* species, *Entamoeba histolytica*, arenaviruses, arboviruses, *Clostridium botulinum*, species of the genus *Candida*, *Vibrio*

*cholera, Cryptococcus neoformans, EHEC strains of E.coli O157:H7, O26:H11, O111:H8 and O104:H21, ETEC strains of E.coli, strains of E. coli shown to possess enteroinvasiveness (EIEC), EPEC strains of E.coli EAggEC strains of E.coli., DAEC strains of E.coli, filoviridae, parvovirus, Filarioidea, Staphylococcus aureus, species of the genus Clostridium perfringens, Helicobacter pylori, Caliciviruses, Giardia lamblia, Neisseria gonorrhoeae, hantaviruses, hepatitis viruses types A, B, C, D, E, Legionellae strains, Mycobacterium leprae, Listeria monocytogenes, species of the genus Clostridium perfringens, Borrelia burgdorferi, Pseudomonas pseudomallei, Epstein Barr virus, Onchocerca volvulus, Poxvirus, Bordetella pertussis, Yersinia pestis, Coxiella burnetti, rabies virus, Treponema pallidum, Mycobacterium tuberculosis, Salmonella typhi, a (eukaryotic parasite) causing malaria, pneumocystis pneumonia, an agent causing toxoplasmosis, or any combination thereof.*

6. A vaccine according to ~~any preceding~~ claim 1 which elicits a protective response against a rotavirus, respiratory syncytial virus, Mycobacterium tuberculosis, human immunodeficiency virus, *E.coli*, *Vibrio cholera*, streptococci and/or chlamydia.

7. A vaccine according to ~~any of the preceding~~ claims 1 wherein the heterologous antigen is a viral and/or bacterial antigen optionally a (gp 160) envelope protein of the HJV virus, a surface glycoprotein of a *Leishmania* parasite, Shiga-like toxin, *Shigella* lipopolysaccharide antigen, *Escherichia coli* fimbrial antigen, a CFA

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antigen of an enterotoxigenic *Escherichia coli* strain, anthrax toxin, pertussis toxin, tetanus toxin.

8. A vaccine according to any of claims 1-4 wherein the heterologous antigen is a human allergen or the heterologous antigen is specific for tetanus.

9. A vaccine according to any of the preceding claims 1 which can induce protective immunogenicity.

10. A vaccine according to any of the preceding claims 1 formulated as a single dose vaccine.

11. A vaccine according to any of the preceding claims 1 wherein the recombinant *Lactobacillus plantarum* expresses the heterologous antigen intracellularly and/or on the cell surface to a degree exceeding that of *Lactobacillus plantarum* 80 expressing  $\beta$ -galactosidase.

12. A vaccine according to any of the preceding claims 1 wherein the recombinant *Lactobacillus plantarum* comprises a homologous expression and/or secretion signal, optionally in an expression vector for *Lactobacilli*, preferably for *Lactobacillus plantarum*.



13. A vaccine according to ~~any of the preceding~~ claims 1 wherein the recombinant *Lacto bacillus plantarum* strain exhibits a persistance (in the individual vaccinated) exceeding 5 days, preferably exceeding 9 days, suitably more than 15 or even 20 days

14. A vaccine according to ~~any of the preceding~~ claims 1 wherein the recombinant *Lactobacillus plantarum* exhibits a persistance longer than that of *L plantarum* 80, preferably longer than that of *L plantarum* NCIMB 8826, under equivalent conditions.

15. A vaccine according to ~~any of the preceding~~ claims 1 formulated administration to a human, such as an infant, immunocompromised person, elderly person or a normally healthy infant, child or adult.

16. A vaccine according to ~~any of the preceding~~ claims 1 wherein the recombinant *Lactobacillus plantarum* is a recombinant *Lactobacillus plantarum* 256.

17. A vaccine according to ~~any of the preceding~~ claims 1 wherein the vaccine comprises at least one adjuvant or a pharmacologically acceptable carrier.

18. A recombinant *Lactobacillus plantarum*, optionally a recombinant strain of *Lactobacillus plantarum* 256, as defined in ~~any of the preceding~~ vaccine claims 1.

23. A *Lactobacillus* organism according to ~~any of~~ claims 18 to 22 which is *L. plantarum* or is for use in a vaccine.

25. A bacterium according to ~~any of~~ claims 19 to 24 for use in a method of prophylaxis or treatment of the human or animal body.

28. The use of a bacterium according to ~~any of~~ claims 19 to 24 in the manufacture of a vaccine.

30. The use according to ~~any of~~ claims 26 to 29 for treating or preventing tetanus.